Endothelial cells derived from embryonic stem cells respond to cues from topographical surface patterns.

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Public Summary:
The generation of micro- and nano-topography similar to those found in the extra cellular matrix of three-dimensional tissues is one technique used to recapitulate the cell-tissue physiology found in the native tissues. Despite the fact that ample studies have been conducted on the physiological significance of endothelial cells alignment parallel to shear stress, as this is the normal physiologic arrangement for healthy arterial EC, very few studies have examined the use of topographical signals to initiate endothelial cell alignment. Here, we have examined the ability for our mouse embryonic stem cell-derived endothelial cells (ESC-EC) to align on various microchip topographical systems. Briefly, we generated metal molds with 'wrinkled' topography using 1) 15 nm and 2) 30 nm of gold coating on the pre-strained polystryene (PS) sheets. After thermal-induced shrinkage of the PS sheets, polydimethylsiloxane (PDMS) microchips were then generated from the wrinkled molds. Using similar ShrinkTM-based technology, 3) larger selectively crazed acetone-etched lines in the PS sheets, and 4) fully crazed acetone-treated PS sheets of stochastic topographical morphology were also generated. The 15 nm and 30 nm gold coating generated 'wrinkles' of uniaxial anisotropic channels at nano-scaled widths while the crazing generated micron-sized channels. The ESC-EC were able to respond and align on the 320 nm, 510 nm, and the acetone-etched 10.5 [unknown]m channels, but not on the fully 'crazed' topographies. Moreover, the ESC-EC aligned most robustly on the wrinkles, and preferentially to ridge edges on the 10.5 mum-sized channels. The ability to robustly align EC on topographical surfaces enables a variety of controlled physiological studies of EC-EC and EC-ECM contact guidance, as well as having potential applications for the rapid endothelialization of stents and vascular grafts.

Scientific Abstract:
The generation of micro- and nano-topography similar to those found in the extra cellular matrix of three-dimensional tissues is one technique used to recapitulate the cell-tissue physiology found in the native tissues. Despite the fact that ample studies have been conducted on the physiological significance of endothelial cells alignment parallel to shear stress, as this is the normal physiologic arrangement for healthy arterial EC, very few studies have examined the use of topographical signals to initiate endothelial cell alignment. Here, we have examined the ability for our mouse embryonic stem cell-derived endothelial cells (ESC-EC) to align on various microchip topographical systems. Briefly, we generated metal molds with 'wrinkled' topography using 1) 15 nm and 2) 30 nm of gold coating on the pre-strained polystryene (PS) sheets. After thermal-induced shrinkage of the PS sheets, polydimethylsiloxane (PDMS) microchips were then generated from the wrinkled molds. Using similar ShrinkTM-based technology, 3) larger selectively crazed acetone-etched lines in the PS sheets, and 4) fully crazed acetone-treated PS sheets of stochastic topographical morphology were also generated. The 15 nm and 30 nm gold coating generated 'wrinkles' of uniaxial anisotropic channels at nano-scaled widths while the crazing generated micron-sized channels. The ESC-EC were able to respond and align on the 320 nm, 510 nm, and the acetone-etched 10.5 [unknown]m channels, but not on the fully 'crazed' topographies. Moreover, the ESC-EC aligned most robustly on the wrinkles, and preferentially to ridge edges on the 10.5 mum-sized channels. The ability to robustly align EC on topographical surfaces enables a variety of controlled physiological studies of EC-EC and EC-ECM contact guidance, as well as having potential applications for the rapid endothelialization of stents and vascular grafts.